THE

Hindu Message

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from the Hindu Standpoint

Medical Supplement

'चिकित्सितात्पुण्यतमं न किञ्चिदपि शुश्रुमः'। 'बिभेत्यल्पश्रुताद्वेदो मामयं प्रहरिष्यति'

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NOTES AND COMMENTS.

Dr. Davison cites the case of a man, aged 41 who had asthma for twenty-two years. For several years attacks occured in the spring and fall only and lasted from seven to fourteen days. These attacks gradually increased in severity and frequency till wheezing was present practically the entire year and the acute attacks occured during all seasons. Cutaneous tests were made with protein extracts from all the different foods the patient ate throughout the entire year and all were negative. The extract from dog hair gave a strongly positive reaction. Further questioning of the patient brought out the fact that the attacks of asthma occurring in the spring and fall had usually been after hunting trips and that his dog now slept on the steps of his sleeping porch just by the patient's bed. The dog was sent away and attacks ceased at once. To give this diagnosis a rational test, a lapse of two weeks was allowed. At the end of two weeks, a neighbor's dog was borrowed and patient played with it for five minutes. Fifteen minutes later a severe attack of asthma began.

* * *

The Government of Bengal has sanctioned Rs. 17,000 for experimenting with tube wells, which is a move in the right direction. The tube well is no doubt one of the cheapest and most efficient means of obtaining water, but it is not a system which can be universally adopted. The existence of a local supply of water underground can only be definitely ascertained by experiments.

* * *

We are sorry to learn of the death of the famous Japanese analytical chemist, Jokichi Takamine. Takamine discovered the diastatic enzyme known as taka-diastase, used as starch digestant, and isolated the active principle of suprarenal glands, known as adrenalin. He was the consulting physician of Messrs. Parke Davis & Co.

* * *

The variation in the pulse rate is so great that it does not seem practical to discuss it in detail at this time. Perhaps the two prinicipal factors to be considered when observing the rate of the pulse are the peripheral resistance and condition of the heart. In tachycardia, paralysis of the vagus or stimulation of the sympathetic or cardiac ganglia, should be considered, while in bradycardia, just the opposite condition, stimulation of the sympathetic or cardiac ganglia may be the exciting cause. A slow pulse may be found during the convalescence from typhoid fever, pneumonia, the acute infectious fevers, hemorrhages, injuries to the cervical portion of the spinal cord and, in conditions which cause a continuous stimulation of the vagus centers. A rapid pulse is found in fevers, vague neuritis, exophthalmic goiter, intense excitement, emotional states, failing compensation and in valvular lesions of the heart. A slow pulse in colic and a rapid pulse in peritonitis. This may be valuable in making a differential diagnosis. Both the rapid and slow pulse give us only a hint as to just what the real trouble may be. In such cases the physician will have to apply best means and methods that he may have at his command to complete the diagnosis.

* * *

Dr Lian concludes that from observations of the oculo cardiac reflex (slowing of the pulse on compression of the eyeballs) which was positive in a large proportion of his cases of asthma, that bogus hypertonus is an important factor in the asthma syndrome. This theory naturally suggests the use of belladonna in treatment, and in his hands, with sufficiently large doses, this drug has given remarkably satisfactory results. He regards adrenalin (which acts by stimulation of the sympathetic) as the proper drug for the actual crisis, but he believes that belladonna is capable of preventing the crisis from occurring.

Fatty Acids in the treatment of Diseases caused by Acid Fast Germs.

By CATAIN P. GANGULI, B. A., D. T. M.

The object of writing this thesis is to introduce fatty acids as a therapeutic agent in the treatment of diseases caused by acid fast germs. Marxer was the first man to experiment with sodium oleate in tuberculosis. In 1917-18, Sir L. Rogers advocated the use of fatty acids of various oils in leprosy and tuberculosis. In August 1919, I got permission from Col. Macrae, O. C., I. S. H., Quetta, to investigate the action of Sodium Morrhuate and Gynocardate in leprosy and tuberculosis. In the same year, Col. Sutherland inspected these cases and gave a favourable report. At the end of the year, I submitted my first report on tuberculosis, which was published in the Indian Medical Gazette of April 1920. The report on the action of fatty acids on leprosy was submitted later and was published in the Indian Medical Gazette in August 1920. I owe my grateful thanks to Col T. G. F. Paterson, D. S. O., I. M. S, who gave me special facilities to investigate on this matter, by creating a special Tuberculosis ward of 24 beds and a leprosy ward of 12 beds. Seventy-seven cases of leprosy were investigated in this way. The clinical results were more satisfactory.

It must be confessed that the dry climate of Qettta was an ideal place for a sanatorium and was remarkably free from dust unlike other places of Baluchistan. The dietetic factor was no less important. Large quantities of pure milk and cream were given to the patients to supply the calcium, so essential for the calcification of tubercular foci. Intestinal and systematic antisepsis were attempted with nascent chlorine chiefly with a view to control the effects of intestinal stasis, due generally to pendulous cœcum.

The fact that tuberculosis generally affects the mesoblastic tissues of human beings and leprosy prefers the epiblastic tissues raises the question of inherent deficiency in adrenalin or thyro-iodine of the patient suffering from these diseases. These endocrine glands have got remarkable controlling influences over the susceptibility of these tissues to various diseases.

In the following chapters, I have laid particular stress on the treatment of the diseases from clinical point of view. A patient was only declared cured when his condition was improved, the acid fast bacilli disappeared from the sputum. Sputum became free of albumin and no reaction followed after administration of Koch's old tuberculin.

I have been using ethyl esters of various fatty acids since last year and a half and with the improvement of manufacturing processes, it has become absolutely safe to give these drugs intravenously. I must gratefully acknowledge my thanks to Col. Bernardo for giving me new ideas and conceptions as to the etiology and treatment of the diseases. The following pages however contain my own ideas, experiences and experiment in connection with the treatment of the diseases caused by acid-fast germs.

EVOLUTION.

Chaulmugra oil was a known remedy for leprosy from pre-historic ages. We find it mentioned in the *Ayurvedas*, the Hindu medical books, supposed to be written before 1000 B. C.

Again we find mention of other oils, viz., *Nim* oil or oleum Margosa and *Gurjan* oil in the *Ayurvedas*, whose virtues were extolled in the treatment of various skin diseases, especially syphilis and leprosy.

The methods of administration of all these drugs were chiefly oral and by inunction. The first effort of more efficient administration was adopted by Dr. Heisser, who recommended intramuscular injection of chaulmugra oil in the treatment of leprosy; but this method was very painful and slow in its action, although it was decidedly more efficacious than the other methods.

Although the etiological factors of leprosy and tuberculosis were solved by Hansee and Koch in 1871 and 1882 respectively, the nature and peculiarities of lepra and tubercle bacilli were imperfectly understood before 1905 when Dycke published the results of his laborious researches. His conclusions were as follows:—

1. The parasitic nature of the bacilli were due to a fatty substance in their body.

2. The natural fats, with which the bacilli are impregnated, confer the great resisting powers on them, while the special staining properties were due to fatty acids.

3. The antibodies normally existing in the serum or subsequently produced by action of the disintegrated bacteria are unable to penetrate the fatty envelopes of becteria.

He succeeded in extracting a fatty principle, called *Nastin*, from cultures of lepra-streptrotrix which is biologically identical with the fatty substance contained in lepra bacilli. *Nastin* produces partial antibodies for fatty substance so that the other partial antibodies for the bacillary protein may totally disintegrate the bacilli. This was the first attempt for therapeutic use of fat in a rational manner.

Later on, he extracted a similar fatty principle from tubercle bacilli which he named Tuberculo-Nastin. He was able not only to produce, by its injection, focal reactions, but also got unmistakable evidences of disintegrttion of tubercle bacilli. Subsequently he introduced different combinations of Nastin and Benzoil chloride which he named Bastin Bo, B1. and B2. These were somewhat successful in the treatment of leprosy, but fell into disuse on account of high cost and inconstancy of action. In 1911, Marxer put sodium and oleate to clinical test and found favourable result.

In the year 1915, Sir Leonord Rogers carried out his idea of isolating the most active principle of chaulmugra oil and injecting it in lepra cases. First, he tried the effect of the sodium salt of a fatty acid of a lower melting point contained in that oil. The effects were remarkable and both focal and general reactions were noticed in some cases within 24 hours after intravenous admmistration. Later on, he found that the sodium salts of the fatty acid of the oil having higher melting points were still more useful; so he mixed the sodium salts of all these acids and named the mixture Sodium Gynocardate "A', and later on more correctly Sodium Hydnocarpate.

Dr. K. K. Chatterji of Calcutta began to use the ethyl ester of margosic acid got from Nim oil in leprosy and reported some good results. He

has also introduced a diagnostic procedure from difference in hæmolysis observed by treating sodium margosate with washed erythrocytes of syphilitic and non-syphilitic subjects. This opens out a new chapter for a similar diagnosis of tubercle patients.

Just as chaulmugra oil was a long known remedy for leprosy, codliver oil enjoyed a great reputation of having favourably influenced the treatment of consumption. Consumption is a wasting disease and is marked by a gradual consumption of fat in the body. Codliver was known to be the most easily assimilable form of fat existing and it was given with the idea of replacing some of the fat lost through consumption. It was Sir Rogers who first discovered that besides its food-value the fatty acid of codliver oil possessed marked bacteriolytic properties which was specially active against acid-fast organisms. He extracted the unsaturated fatty acids from codliver oil and injected them in the form of sodium salts in tubercle and leprosy patients and got conclusive evidences of marked focal and general reactions as well as of bacteriolysis. In some respects its action was superior to sodium hydnocarpate as less toxic and more rapid in its action.

During my investigation in the years 1919-20, I was compelled to fall on sodium hydnocarpate treatment in tuberculosis, as sodium morrhuate was not available in the market for three months. I found that sodium hydnocarpate with all its drawbacks was also successful in the treatment of tuberculosis. I also found that sodium morrhuate had got another remarkable property, namely fibrolytic action, specially in connection with newly formed fibrous tissues formed by flattering up of epitheloid cells in tubercular foci. I submitted my first report on the 31st December 1919 and the second on the 20th January, 1930.

Professor Dean of Hawaii also prepared an ethyl ester from chaulmugra oil which was given an extensive trial in the treatment of leprosy in the leper colonies of Hawiian island. Extraordinary success had been achieved in this respect.

Sir. L. Rogers began to use ethyl ester of morrhuic acid in 1919 on both tubercle and leprosy patients and found that it was not painful and was very easily assimilated if injected subcutaneously. Thus a possibility of a method of a being extensively used in ordinary outdoor dispensaries, in the treatment of leprosy and afbrile tuberculosis has been obtained, for the best results of sodium morrhuate and hydnocarpate were obtained by the intravenous method.

Later on, a most important discovery was made by Rogers, who discarded the exclusive specificity of action of cod liver oil and chaulmugra oil and pronounced fatty acids are more or less specific against acid-fast germs. He has undertaken to find out most potent form from various fatty acids. With the assistance of Dr. S. Ghosh, he prepared some fatty acids from soya beans and sardine oils and got some excellent results.

Dr. Minchin's thesis on the efficacy of allyl sulphate on lupus and tuberculosis of lungs prompted the use of allyl ester of morrhuic acid but it is found to give rather severe reaction and produces a condition of prolonged hyper-susceptibility.

In August 1920 Dr. J. A. Shaw-Mackenzie advocated the use of fatty acid in cancer therapy; he had previously established tipolytic or fat splitting ferment in the tissues was an important factor in the defence of the body against cancer and bacterial invasions.

Dr. Muir introduced E. C. C. O. containing Ethyl ester of fatty acids of camphor, creasote and olive oil in proportions of 1, 1, 1 and 2½ which is absolutely painless in subcutaneous injection. He got unmistakable evidences of febrile reactions in majority of his leprosy cases followed by breakdown of bacilli into fragments in cases showing severe reactions.

HYPOTHESIS.

We should understand the underlying principles related to the specific nature of the action of fatty acids, for, on the correct understanding of the hypothesis depend the posology, which must be adopted to the different symptoms exhibited during the course of treatment.

The fatty acids act in three ways:—

1. *Antisepsis.* 2. *Bacteriolysis-* 3, *Fibrolysis*

1. Antesepsis:—The first action of fatty acid is of an antiseptic nature.

In Vitro experiments:—

(1) 5c. c, of 3 per cent solution of sodium hydnocarpate and 5 c. c. emulsion of Tubercle bacilli are kept in incubator for 24 hours. The mixture is centrifugalised and the sediment is washed with sterile saline solution. This process is repeated three times, so that the tubercle bacilli are freed from soap. Inoculation on Dorset's egg medium and potato medium with this sediment failed to grow tubercle bacilli.

(2) The same experiments were done leaving the mixture for 12, 10, 8, 6, and 4 hours. There were failure of cultures in Dorset's egg medium after treatment for 12 10, 8 and 6 hours in sodium morrhuate, but one out of 4 cultures were successful in case of residues after treatment for 4 hours in sodium morrhuate.

In vivo experiments:—

Series 1, Emulsions of residues after 24, 12, 8, 6 and 4 hours incubation were injected into the peritoneal cavities of guineapigs. None of the guineapigs except those treated with residues after 4 hour's incubation died, although all of them showed enlargement of mesenteric glands.

Series 2. No subcultures from these enlarged glands of spleen were successful except those from the guineapigs which died.

The above experiments clearly proved the antiseptic nature of sodium so far as tubercle bacilli are concerned. Sunlight is the most powerful factor in killing the bacilli but this was avoided by putting the tubes in the incubator.

The H-ion concentration of the solution of sodium morrhuate was not examined in the above experiments.

By the injection of sodium morrhuate *an atmosphere* is created in the tubercular focus by which the flourishing of the germs is inhibited to a certain extent. An amelioration of symptoms is thus produced from the diminished production of toxins secreted by the germs. These toxins are responsible for the production of fever, headache, malaise, quickness of heart beat, pain in the chest, nervous irritations, loss of appetite, etc. I must say that like

various other chemical antiseptic drugs, such as, creosote, pinol, eucalyptus oil, etc, the value of fatty acids as antiseptic is very limited indeed.

2. *Bacteriolysis*:—In vitro experiment—Emulsion of T. B. 5 c. c. and sod. morrhuate 9 per cent 5 c. c.—Incubated for 10 days. The bacilli did not lose acid character, although they became slightly more pink in colour, by counter stain with Methylene blue. Hence there is no *direct* bacteriolytic effect. Now let us see whether it has got any indirect one.

In 1917, Jobling Peterson declared that intravenous injection of vaccines produced a mobilisation of serum *protease* and *lipase* and that for the destruction of lipoid-rich organism, such as tubercle and lepra bacilli, the fat-splitting ferment are essential. The researches of Shaw Mackenzie experimentally proved that sodium olrate, morrhuate and gynocardate exert marked accelerating action on the lipase of extract of pancreas. He also proved that the addition of sodium oleate to carcinomatous serum removed the inhibitory action of such serum in lipase. The most important question is to decide whether the fatty acids have got any specific action in the production of immunity. The following facts have been established from clinical observations:—

(1) Fatty acids produce *Focal* and *General* reactions in persons suffering from active tubercular and leprous processes.

(2) No reaction is obtained in healthy individuals, if treated with fatty acids.

Focal reaction:—This is most readily observed in lupus and leprosy cases. In the former the nodules become shining and hyperæmic generally within two days after injection and this is followed by drying up and formation of scabs. If this process is repeated the scabs become thicker and when they peel off, a healthy and rosy scar tissue is all that is left of the nodule. In some cases, scaly exfoliation follow hyperæmia. In open tuberculous surgical cases like psoas abscess, sinuses leading to caseating glands, etc., there are first an increase in the discharge of pus followed quickly by decrease till they are healed up.

Similarly focal reactions may be manifested in pulmonary tuberculosis by the increase of the quantity of expectoration, pain and feeling of tenderness over the affected parts. In a limited number of cases, hæmoptysis occurred during reaction pointing congestion of the tubercular foci.

General reaction:—General reaction as shown by objective symptoms, such as pyrexia, pulse, respiration or loss of weight, etc., were observed after about 4000 intravenous injections of sodium Morrhuate in 77 hospital and 20 private cases. A study of the reaction is absolutely convincing that fatty acids are remarkably potent drugs and that doses should be very carefully regulated especially in febrile sensitive cases. General reaction was noted especially in the early cases of pulmonary tuberculosis with relatively large involvement of the lung tissue. The reaction was most severe in bad cases of progressive type, in worst cases the febrile reaction was nil probably due to paralysis of reacting tissues by over-stimulation by the toxic products.

It was remarkable how these reactions are closely allied to those induced by tuberculosis and serve to establish the specific nature of the two fatty acids. In asserting this, I hope, I may not be misunderstood. Fatty acids cannot be certainly regarded as true toxins, nor can the reaction mentioned above be explained as directly due to anaphylaxis or excitement of anaphylotoxins in the body, as fatty acids are not proteins. But though the existence of specific antibodies after exhibition of Tuberculin has been established in the affected persons, the failure of doing so in healthy subjects is proof positive that Tuberculin also is not a true toxin. Hence we see that both Fatty Acids and Tuberculin produce specific reactions in diseased persons although both the substances are not true toxins, still there is no doubt about the existence of some of the antibodies (in the shape of antitoxins, opsonins, aglutinins, and complement-fixing antibodies) in tubercular patients specially treated with bacillary substances.

It has been already noted, that the peculiar reacting power of acid-fast bacilli are due to the fatty substances which they are impregnated. The bacillary emulsion is supposed to make demands for production of various antibodies for various substances of which they are composed. The minute quantity of fat present in the bacillary emulsion excites the formation of insufficient quantity of partial antibodies for the bacillary fatty substances and it may not be unjustifiable to presume that the insufficient quantity of lipase or lypolysin is a serious factor against the rapid formation of lysins for bacillary substances which are mainly protein in nature. In fact, in my opinion, the action of both these bodies are interdependent on one another and the lypolytic factor is the more important armour in depriving the germs of their potent and proteolysis is dependent on lipolysin.

The injection of fatty acids removes the inhibitory action of serum on lipase and accelerates the fat-splitting activity of lipase in the serum, which becomes low in all sorts of chronic bacterial invasion. It also excites in my opinion, the production of more than requisite amount of partial antibodies for bacillary fats. The beeded appearance of the bacilli, which is due in my opinion to the disintergration of the fatty substances in their body, is a frequent phenomenon in the cases treated with fatty acids. But ordinarily it appeared after pretty big doses had been administered.

Again it had been frequently observed that in afebrile cases., no reactions were visible until a big dose had been reached, and sometime it was concomitant with the beeded appearance of the bacilli. This shows that the proteolytic action commenced after the lypolytic action had been established through formation of sufficient quantity of lipolytic antibodies. I had lately been trying to substantiate those hypothesis by serological experiments but facilities in the shape of laboratory and specially treated patients are wanting at present.

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To be continued.

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